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# Prognostic Significance of Severe Interstitial Edema With Minimal Infiltrate in Renal Allograft Biopsies

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**O**CCASIONALLY, percutaneous renal allograft biopsies show severe localized or diffuse interstitial edema with only minimal interstitial infiltrate. Based on diagnostic features such as intimal arteritis, tubulitis, and/or infiltrate in other areas of the biopsy, in many cases a histological diagnosis of acute rejection (AR) can be made, but in biopsies in which no arteries are found the diagnosis often remains uncertain. We tested whether severe edema with little or no infiltrate in (part of) the biopsy (1) is associated with acute and/or chronic rejection; (2) is associated with an unfavorable response to treatment and a higher incidence of graft failure, with implications regarding the indication for antirejection therapy; and (3) can be related to other histological features.

## MATERIALS AND METHODS

Consecutive allograft biopsies, taken over a period of 3 years (1988–1990), were scored in a blinded way according to the guidelines of Banff classification<sup>1</sup> and screened for the presence of severe interstitial edema. Edema was defined as a cortical area in which at least 10 adjacent tubuli were separated by intertubular spaces of more than one tubular diameter in width and filled with serous fluid in which no or only a few mononuclear cells were present. Graft survival rates of the kidneys with severe edema were compared to those in the control group, consisting of all cases in the series that were histologically classified in the same Banff categories as the edema group and that had undergone similar treatment.

## RESULTS AND DISCUSSION

In a series of 292 consecutive adequate renal graft biopsies, 26 cases (8.9%) showed areas of severe hypocellular edema, which were localized in 20 cases and diffuse (ie, over more than 80% of the biopsy area) in six cases. In 24 of 26 cases, the histological diagnosis was AR, Banff classification grade I (n = 5), grade II (n = 10), and grade III (n = 9). The two remaining cases showed borderline changes with minimal tubulitis, in one case accompanied by membranous nephropathy and transplant glomerulopathy and in both cases by interstitial fibrosis suggestive of chronic rejection. In 13 of 26 biopsies with edema, medium-sized or larger arteries were seen; and in 12 cases (92%) these showed intimal fibrosis, which in 9 of 12 was accompanied by acute intimal arteritis. One biopsy contained arteries without pathological changes. Apart from the case with membranous nephropathy, all patients received antirejection therapy. As a control group for statistical evaluation of graft survival, we chose all grafts in the 3-year series with a histological diagnosis of either borderline changes or AR grades I

through III and in which antirejection therapy had been given. The diagnoses in the control group (total n = 86) were borderline changes (n = 12), AR grade I (n = 17), grade II (n = 49), and grade III (n = 8). In the edema group, the percentage of graft failure due to rejection within 12 months was 26.3%, and within 3 years it was 41.7%. In the control group, these figures were 17.3% and 22.4%, respectively ( $P < .02$ , log rank test).

The finding, in our series, that severe hypocellular edema in renal allograft biopsies is associated with a higher incidence of immunological graft failure is likely related to the higher incidence of grade III AR in the edema group (9 of 26 vs 8 of 86 in the control group;  $P < .004$  Fisher exact test). Consistent with this is the high incidence of intimal arteritis. In the edema group, the intimal arteritis is in all cases accompanied by intimal fibrosis. This could imply that hypocellular edema is associated with impaired circulation, causing obstruction of cellular influx. Such obstruction is more likely to be severe when acute intimal arteritis is superimposed on intimal fibrosis. The continuing higher incidence of graft loss over several years in the edema group, despite antirejection therapy, may also indicate that there is a relation to chronic vascular damage. Whether the presence of hypocellular edema gives additional prognostic information in those cases that show signs of acute and/or chronic vascular rejection, and especially whether it is a sign of vascular obstruction in biopsies without representative vessels, remains to be studied in a larger series.

We conclude that in renal allograft biopsies, areas of severe hypocellular edema are an unfavorable diagnostic sign, probably due to vascular obstruction and often caused by a combination of acute and chronic rejection. They are associated with an increased risk of immunological graft failure. There is, however, insufficient indication for withholding antirejection treatment.

## REFERENCES

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